Eastern Equine Encephalitis (EEE)

Section 1: ABOUT THE DISEASE

A. Etiologic Agent

Eastern equine encephalitis (EEE) virus is a member of the family *Togaviridae*, genus *Alphavirus*. It is generally spread to humans by mosquitoes. Viruses transmitted by mosquitoes are referred to as arthropod-borne viruses, or arboviruses. EEE virus is one of more than 30 arboviruses known to infect humans in the Western Hemisphere. Because of the severity of the disease and the high case-fatality rate associated with EEE, it is considered one of the more serious arboviral diseases in the U.S.

B. Clinical Description

EEE virus infection may result in an acute febrile illness of variable severity, with neurologic symptoms ranging from headache to encephalitis (inflammation of the brain), coma, and death. The first symptoms of EEE generally include a sudden onset of high fever (103–106°F), stiff neck, headache, and lack of energy. In the more severe EEE cases, seizures, coma, and death may develop rapidly. As many as one-third to one-half of EEE cases are fatal (most fatalities occur during acute illness, but some result from severe, persistent complications of infection), with those under 15 and over 50 years of age at greatest risk for severe disease. Many people who survive EEE develop residual, long-term, mild to severe neurologic deficits.

C. Vectors and Reservoirs

Certain species of birds serve as the reservoirs for EEE virus. Mosquitoes spread the virus from one bird to another. Several species of mosquito can become infected with EEE virus, but the most important species in maintaining the bird-mosquito-bird transmission cycle is *Culiseta melanura*. Some mosquitoes prefer to feed on birds while others feed on both birds and mammals (e.g., humans and horses). If a mosquito bites an infected bird and then bites a person, that person may become infected. People, horses, and most other mammals are considered "dead-end" or incidental hosts, and they do not appear to play a role in the maintenance of EEE virus in the environment.

D. Modes of Transmission

EEE virus is spread to humans by the bite of an infected mosquito. Direct person-to-person transmission of EEE does not occur. There is no evidence to suggest a person can get EEE virus infection from handling a live or dead infected bird or animal. However, EEE is known to be spread from bird-to-bird in flocks of ratites (emus, ostriches, and rheas). Ratites are large, flightless birds from Australia, Africa, and South America, sometimes raised in the Northeast as livestock or zoo animals. In these birds, EEE virus infection causes a syndrome characterized by gastroenteritis and hemorrhage, and blood and feces may contain large quantities of virus. Therefore, while transmission to humans through blood and/or feces has not been documented, strict precautions should be taken when handling sick or dying ratites infected with EEE virus and their secretions or excretions. Gloves or double plastic bags should be used when handling dead animals infected with EEE virus that are not ratites.

E. Incubation Period

The incubation period for EEE is 3–10 days.

F. Period of Communicability or Infectious Period

EEE virus infection is not communicable from person to person.

G. Epidemiology

Signs of equine (horse) encephalitis were first noted in the eastern U.S. as early as 1831. Over 100 years later, the etiologic agent EEE virus was recovered from a horse brain in 1933. The virus was first isolated from a human case in 1938 during an outbreak in southeastern Massachusetts. EEE virus is found in the eastern and north central regions of the U.S. and adjacent regions of Canada, as well as in portions of Central and South America. The greatest risk of acquiring EEE virus infection is from late July through September (until the first frost). The risk is highest in southeastern New England, especially in coastal regions. Since 1964, there have been more than 200 confirmed cases of EEE reported nationwide. Between 1938 and 2004, 79 human cases of EEE were reported in Massachusetts. The majority of these cases occurred in Plymouth, Norfolk, and Middlesex counties.

H. Bioterrorist Potential

While this pathogen is not considered to be of risk for use in bioterrorism, the Centers for Disease Control and Prevention (CDC) lists the EEE virus as a Category B bioterrorist agent.

Section 2:
REPORTING CRITERIA AND LABORATORY TESTING

A. What to Report to the Massachusetts Department of Public Health (MDPH)

Report any case of EEE virus infection diagnosed by a health care provider, with or without supporting laboratory results.

B. Laboratory Testing Services Available

The MDPH State Laboratory Institute (SLI) is able to perform immunoglobulin G (IgG) and immunoglobulin M (IgM) enzyme immunoassay (EIA) tests for eastern equine encephalitis virus (EEEV). Cerebrospinal fluid (CSF) and brain tissue can also be tested for EEEV by cell culture and antigen detection with indirect fluorescent antibody and real-time detection polymerase chain reaction (RTD-PCR).

For additional information on submitting samples or testing for other types of arboviral infection, contact the SLI Viral Serology Laboratory at (617) 983-6396 or the SLI Virus Isolation Laboratory at (617) 983-6382.

Section 3:

REPORTING RESPONSIBILITIES AND CASE INVESTIGATION

A. Purpose of Surveillance and Reporting

- To identify locally acquired cases of EEE virus infection in humans to better understand the local epidemiology of EEE virus.
- To identify locally acquired cases of EEE virus infection in humans to help target mosquito control and public health education efforts.
- To monitor trends in EEE incidence in order to make inferences concerning levels of risk over time.

B. Laboratory and Health Care Provider Reporting Requirements

EEE is reportable to the local board of health (LBOH). The MDPH requests that health care providers immediately report to the LBOH in the community where the case is diagnosed, all confirmed or suspect cases of EEE, as defined by the reporting criteria in Section 2A. If this is not possible, call the MDPH Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850.

Laboratories performing examinations on any specimens derived from Massachusetts residents that yield evidence of EEE infection shall report such evidence of infection directly to the MDPH within 24 hours.

For questions related to EEE in animals or to report a suspect case of EEE virus infection in an animal, contact the Massachusetts Department of Agricultural Resources (MDAR), Division of Animal Health, Dairy Services, and Biosecurity (DAH) by telephone at (617) 626-1795 or by fax at (617) 626-1850.

C. Local Board of Health (LBOH) Reporting and Follow-Up Responsibilities

Reporting Requirements

MDPH regulations (*105 CMR 300.000)* stipulate that EEE is reportable to the LBOH and that each LBOH must report any case of EEE or suspect case of EEE, as defined by the reporting criteria in Section 2A. Cases should be reported to the MDPH Bureau of Communicable Disease Control, Office of Integrated Surveillance and Informatics Services (ISIS) using an official MDPH *Arbovirus Case Report Form* (found at the end of this chapter). Refer to the *Local Board of Health Reporting Timeline* at the end of this manual's *Introduction* section for information on prioritization and timeliness requirements of reporting and case investigation.

Under *105 CMR 300.140, Reporting of Animal Diseases with Zoonotic Potential by Veterinarians,* any veterinarian or LBOH with knowledge of an animal disease potentially infectious to humans must also report the disease to the DAH. Specific diseases in animals which veterinarians must also report directly to MDPH are anthrax, plague, West Nile virus infection (WNV), and Eastern equine encephalitis (EEE) virus infection.

Case Investigation

If a LBOH learns of a suspect or confirmed case of EEE virus infection, it should immediately call the MDPH Division of Epidemiology and Immunization with initial information, any time of the day or night, at (617) 983-6800 or (888) 658-2850.

1. Once the case has been confirmed through laboratory testing at MDPH, the LBOH may be asked to assist in completing an official MDPH *Arbovirus Case Report Form* (found at the end of this chapter) by interviewing the case and others who may be able to provide pertinent information. Most of the information required on the form can be obtained from the health care provider or from the medical record. Use the following guidelines to assist in completing the form:
   a. Demographic information: Accurately record the contact information on the case, as well as the case's age, sex, race, and occupation.
   b. Clinical information: Note the symptom onset date and check off all reported symptoms. Also note whether the case is pregnant. Record whether the case was hospitalized, including location, associated dates, and physician contact information.
   c. Laboratory information: Check off all appropriate tests performed, and attach a copy of any laboratory results.
   d. Information relevant to control and prevention: It is extremely important to accurately record the case's travel history by determining the date(s) and geographic area(s) traveled to by the case within 30 days prior to onset of illness. Also complete the vaccination and disease history sections.
2. If you have made several attempts to obtain case information but have been unsuccessful (e.g., the case or health care provider does not return your calls or respond to a letter, or the case refuses to divulge information or is too ill to be interviewed), please fill out the form with as much information as you have gathered. Please note on the form the reason(s) why it could not be filled out completely.
3. After completing the case report form, attach laboratory report(s) and fax or mail (in an envelope marked "Confidential") to ISIS. The confidential fax number is (617) 983-6813. Call ISIS at (617) 983-6801 to confirm receipt of your fax. The mailing address is:

MDPH, Office of Integrated Surveillance and Informatics Services (ISIS)
305 South Street, 5th Floor
Jamaica Plain, MA 02130
Fax: (617) 983-6813

4. Institution of disease control measures is an integral part of case investigation. It is the responsibility of the LBOH to understand, and if necessary, institute the control guidelines listed in Section 4.

Section 4:
CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements *(105 CMR 300.200)*

Minimum Period of Isolation of Patient

None.

Minimum Period of Quarantine of Contacts

None.

B. Protection of Contacts of a Case

None.

C. Managing Special Situations

Locally Acquired Case

If you suspect that the case acquired the infection locally—because, for example, the person does not have recent travel history to an endemic area or country—it may be necessary to investigate local risk factors for viral transmission or to conduct surveillance for other people with the illness. See Section 4D for more information.

Reported Incidence Is Higher Than Usual/Outbreak Suspected

If the number of cases of EEE reported in your city/town is higher than usual or if you suspect an outbreak, contact the epidemiologist on-call at the MDPH Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850. The situation may warrant an investigation of clustered cases or implementation of prevention and control measures (e.g., enhanced mosquito control). The MDPH Division of Epidemiology and Immunization can help determine a course of action to prevent further cases and can perform surveillance for cases across town lines, which would otherwise be difficult to identify at the local level.

D. Preventive Measures

Environmental Measures

People should be encouraged to reduce mosquito populations around their home and neighborhood by getting rid of any standing water to reduce mosquito breeding. Mosquitoes will begin to breed in any puddle or standing water that lasts for more than four days. People should be advised of the following:

- Dispose of or regularly empty any metal cans, plastic containers, ceramic pots, and other water holding containers (including trash cans) on their property.
- Pay special attention to discarded tires, as stagnant water in tires is a common place for mosquitoes to breed.
- Drill holes in the bottom of recycling containers that are left outdoors, so that water can drain out.
- Clean clogged roof gutters; remove leaves and debris that may prevent drainage of rainwater.
- Turn over plastic wading pools and wheelbarrows when not in use.
- Do not allow water to stagnate in birdbaths; aerate ornamental ponds or stock them with fish.
- Keep swimming pools clean and properly chlorinated; remove standing water from pool covers.
- Use landscaping to eliminate standing water.

Decisions about the need for mosquito control activities (e.g., removing mosquito breeding areas, larviciding, or adulticiding) are normally made by local cities and towns—in conjunction with the local mosquito control district—and are based on mosquito habitat and density, surveillance for EEE virus in mosquitoes, and the number of cases in birds, horses, and humans. In Massachusetts, the MDPH Arboviral Surveillance Laboratory conducts environmental surveillance of mosquitoes at numerous sites for EEE virus as well as for West Nile virus (WNV) (see chapter entitled *West Nile Virus* for more information) and Highlands J virus. Highlands J virus is another mosquito-borne arbovirus which does not cause illness in humans, but it serves as an indicator for the appearance of EEE virus.

Arbovirus surveillance information on birds, mosquitoes, horses, and humans can be accessed on the MDPH website at www.mass.gov/dph.

Your local mosquito control district is an excellent source for information regarding mosquito surveillance and control efforts. If your city or town does not belong to a mosquito control district but is interested in joining one or creating one with other surrounding towns, contact the State Reclamation and Mosquito Control Board, administratively located in the MDAR Pesticide Bureau at (617) 626-1781.

Personal Protective Measures/Education

There is no human vaccine for EEE. People should be advised to take the following precautions if they live in or visit an area with mosquitoes:

- Avoid outdoor activities between dusk and dawn, if possible, as this is the time of greatest mosquito activity.
- Fix any holes in screens and make sure they are tightly attached to all doors and windows.
- Use repellents containing DEET (N,N-diethyl-m-toluamide), and choose a product that will provide sufficient protection for the amount of time spent outdoors. Product labels often indicate the length of time that someone can expect protection from a product. DEET is considered safe when used according to the manufacturer's directions. The efficacy of DEET levels off at a concentration of 30%, which is the highest concentration recommended for children and adults. DEET products should not be used on children <2 months of age. Mosquito netting may be used to cover infant carriers or to protect other areas on children <2 months of age. The following precautions should be observed when using DEET products:
  - Avoid using DEET products that combine the repellent with a sunscreen. Sunscreens may need to be reapplied too often, resulting in an over application of DEET.
  - Apply DEET on exposed skin, using only as much as needed.
- Do not use DEET on the hands of young children, and avoid applying repellent to areas around the eyes and mouth.
- Do not use DEET over cuts, wounds, or irritated skin.
- Wash treated skin with soap and water after returning indoors, and wash treated clothing.
- Avoid spraying DEET products in enclosed areas.

Picardin (KBR 3023) is a relatively new repellent that is now available in the U.S. Recent studies have shown it to be safe and effective. Picardin-containing repellents should be used according to the manufacturer's recommendations.

Permethrin-containing products will kill mosquitoes and ticks on contact. Permethrin products are not designed to be applied to the skin. Clothing should be treated and allowed to dry in a well-ventilated area prior to wearing. Because permethrin binds very tightly to fabrics, once the fabric is dry, very little of the permethrin gets onto the skin.

A number of plant-derived products are available for use as repellents, but most of these products do not provide the same level or duration of protection as products containing DEET. However, there are studies that show that oil of lemon eucalyptus [p-methane 3,8-diol(PMD)] provides as much protection as low concentrations of DEET when tested against mosquitoes found in the U.S.

An EEE Public Health Fact Sheet is available from the MDPH Division of Epidemiology and Immunization or on the MDPH website at www.mass.gov/dph. Click on the "Publications and Statistics" link, and select the "Public Health Fact Sheets" section under "Communicable Disease Control." Additional educational materials are available on the MDPH Arbovirus Information website at www.mass.gov/dph/wnv/wnv1.htm.

ADDITIONAL INFORMATION

The following is the formal CDC surveillance case definition for arboviral encephalitis. It is provided for your information only and should not affect the investigation and reporting of a case that fulfills the criteria in Section 2A of this chapter. (The CDC and the MDPH use the CDC case definitions to maintain uniform standards for national reporting.) For reporting to the MDPH, always use the criteria outlined in Section 2A.

Note: The most up-to-date CDC case definitions are available on the CDC website at www.cdc.gov/epo/dphsi/casedef/case_definitions.htm.

Case Definition: Neurotropic Domestic Arboviral Diseases

The Council of State and Territorial Epidemiologists (CSTE) Position Statement is available on the CSTE website at www.cste.org/ps/2004pdf/04-ID-01-final.pdf.

Clinical Criteria for Diagnosis

Cases of arboviral disease are classified either as neuroinvasive or non-neuroinvasive, according to the following criteria:

Neuroinvasive	Neuroinvasive disease requires the presence of fever and at least one of the following, as documented by a health care provider and in the absence of a more likely clinical explanation: ◆ Acutely altered mental status (e.g., disorientation, obtundation, stupor, or coma); or ◆ Other acute signs of central or peripheral neurologic dysfunction (e.g., paresis or paralysis, nerve palsies, sensory deficits, abnormal reflexes, generalized convulsions, or abnormal movements); or ◆ CSF pleocytosis (increased white blood cell concentration in CSF associated with illness clinically compatible with meningitis [e.g., headache or stiff neck]).
Non-Neuroinvasive	Non-neuroinvasive disease requires, at minimum, the presence of documented fever—as measured by the patient or health care provider, the absence of neuroinvasive disease (above), and the absence of a more likely clinical explanation for the illness. Involvement of non-neurological organs (e.g., heart, pancreas, liver) should be documented using standard clinico-laboratory criteria.

Laboratory Criteria for Diagnosis

Cases of arboviral disease are also classified either as confirmed or probable, according to the following laboratory criteria:

Probable	◆ Stable (less than or equal to a two-fold change) but elevated titer of virus-specific serum antibodies; or ◆ Virus-specific serum IgM antibodies detected by antibody-capture EIA but with no available results of a confirmatory test for virus-specific serum IgG antibodies in the same or a later specimen.
Confirmed	◆ Four-fold or greater change in virus-specific serum antibody titer; ◆ Isolation of virus from or demonstration of specific viral antigen or genomic sequences in tissue, blood, CSF, or other body fluid; ◆ Virus-specific IgM antibodies demonstrated in CSF by antibody-capture EIA; or ◆ Virus-specific IgM antibodies demonstrated in serum by antibody-capture EIA and confirmed by demonstration of virus-specific serum IgG antibodies in the same or a later specimen by another serologic assay (e.g., neutralization or hemagglutination inhibition).

REFERENCES

American Academy of Pediatrics. [Arboviruses]. In: Pickering L.K., ed. *Red Book: 2003 Report of the Committee on Infectious Diseases, 26th Edition.* Elk Grove Village, IL, American Academy of Pediatrics; 2003: 199–205.

CDC. Case Definitions for Infectious Conditions Under Public Health Surveillance. *MMWR.* 1997; 46(RR-10).

Heymann, D., ed. *Control of Communicable Diseases Manual, 18th Edition*. Washington, DC, American Public Health Association, 2004.

"Information on Arboviral Encephalitides." Centers for Disease Control and Prevention. November 7, 2005. <www.cdc.gov/ncidod/dvbid/arbor/arbdet.htm>.

MDPH. *Regulation 105 CMR 300.000: Reportable Diseases, Surveillance, and Isolation and Quarantine Requirements.* MDPH, Promulgated November 4, 2005.

FORMS & WORKSHEETS

Eastern Equine Encephalitis (EEE)

Eastern Equine Encephalitis (EEE)

LBOH Action Steps

This form does not need to be submitted to the MDPH with the case report form. It is for LBOH use and is meant as a quick-reference guide to EEE case investigation activities.

LBOH staff should follow these steps when EEE is suspected or confirmed in the community. For more detailed information, including disease epidemiology, reporting, case investigation and follow-up, refer to the preceding chapter.

- ❑ Immediately notify the MDPH Division of Epidemiology and Immunization, at (617) 983-6800 or (888) 658-2850, to report any suspect case(s) of EEE.
- ❑ To report a case of EEE virus infection in an animal, contact the Massachusetts Department of Agricultural Resources (MDAR), Division of Animal Health, Dairy Services and Biosecurity (DAH) at (617) 626-1795.
- ❑ Obtain laboratory confirmation.
- ❑ Determine whether or not the case was acquired locally, and if so, conduct enhanced surveillance for human illness and investigate local risk factors for viral transmission.
- ❑ If locally acquired, institute mosquito control measures.
- ❑ Fill out the case report form (attach laboratory results).
- ❑ Send the completed case report form (with laboratory results) to the MDPH Bureau of Communicable Disease Control, Office of Integrated Surveillance and Informatics Services (ISIS).